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Pantera Lux Drug Coated Balloon: Twelve-Month Results On The Diabetics Subgroup Of The International DELUX Registry

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Background: In recent years, drug coated balloons have emerged as treatment option for PCI. The present registry aims to evaluate the safety and efficacy of the Pantera Lux Paclitaxel Coated Balloon in a real world setting.
Methods: Between April 2010 and April 2011, 363 diabetic patients were enrolled at 50 sites in 12 countries. Clinical follow-up was performed at 1, 6 and 12 months. The primary endpoint was MACE, a composite of all death, non-fatal MI and clinically driven TVR, at 6 months. Secondary endpoints include MACE at 1 and 12 months. All reported MACE were adjudicated by an independent clinical events committee.
Results: Two hundred fifty-nine men (71.3%) and 104 female (28.7%) with a mean age of 67.4 ±10.2 yrs have been enrolled. One hundred forty-two patients (39.4%) were insulin dependent. Eighty-six patients (23.7%) presented with congestive heart failure and 195 patients (53.7%) had a history of previous MI. The majority of patients presented with stable angina (n=184, 50.7%) followed by unstable angina (n=107, 29.5%). A total of 388 lesions were treated, mainly located in LAD (n=144, 37.1%) and RCA (n=136, 35.1%). The mean reference vessel diameter was 2.9 mm and the mean target lesion length was 15.6 mm. Three hundred forty lesions (87.6%) were in-stent restenotic (ISR) lesions. Thereof 165 lesions were in a BMS (48.5%) and 172 lesions in a DES (50.6%). The majority of ISR lesions were diffuse (n=159, 48.3%, Mehran class II) or focal (n=104, 31.6%, Mehran class I). Follow-up compliance at 6 month follow up is 93.9%. The MACE rate (hierarchical) at 6 months is 11.2% including 11 all death (3.2%, 6 cardiac death [1.8%]), 7 non-fatal MI (2.1%) and 20 clinically driven TVR (5.9%). In 15 cases (4.4%) a target lesion revascularization was needed. Twelve months MACE data will be presented.
Conclusions: Treatment with the Pantera Lux Paclitaxel Coating Balloon showed excellent acute and mid term performance in diabetic patients with mainly ISR lesions. Efficacy and safety are demonstrated by low revascularization rates and low non-fatal MI rate.

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Acute Delivery and Long Term Retention of Sirolimus Nanoparticles Using a Novel Porous Angioplasty Balloon in the Porcine Coronary Model

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Background: Drug coated balloons using Paclitaxel have demonstrated to be clinically effective in selected clinical settings. In contrast, Sirolimus is not easily transferred to the vessel wall using current coating Methods and tissue levels cannot be maintained long enough to control restenosis. In this study, we aimed to evaluate the feasibility of delivery and long term retention of Sirolimus nanoparticles delivered through a novel porous angioplasty balloon in normal porcine coronary arteries.
Methods: A total of 155 coronary arterial segments were treated with a porous angioplasty balloon delivering Sirolimus nanoparticles (Caliber Therapeutics, New Hope, PA) at a 20% overstretch ratio. Coronary angiography was performed at baseline and after delivery to assess safety. Treated coronary segments were harvested immediately after Sirolimus delivery (n=25) and at 4 (n=30), 7 (n=84), 21 (n=7) and 28 days (n=9) and analyzed to detect tissue Sirolimus levels. Distal tissue samples (distal myocardium, lung, liver and kidney) were also collected to determine Sirolimus systemic distribution following local drug delivery.
Results: The Sirolimus levels found immediately after balloon delivery were 422.6±110 ng/mg. Subsequently, Sirolimus tissue levels progressively decreased at 4 (200.13±80.4 ng/mg) and 7 (49.8±17.1 ng/mg) and 21 (32.7±13.6 ng/mg) days. At last follow up (28 days), Sirolimus tissue levels were still above the target therapeutic levels (18.5 ± 9.6 ng/mg). At any given time point, Sirolimus concentrations were >300-fold higher in coronary segments than in distal tissue samples. Drug levels in remote tissues were undetectable after 7 days.
Conclusions: The local arterial delivery of Sirolimus nanoparticles using a novel porous balloon delivery system was safe and capable of achieving long term intra-arterial drug levels without significant systemic residual exposure in a porcine model.

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Luminal Fibrin as a Key Component in Mechanism of Action in Drug Coated Balloon Technologies

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Background: The mechanism of action of Drug Coated Balloons (DCB) is not fully understood. It's suggested that following balloon dilatation, Paclitaxel is deposited on the vascular luminal surface and serves as a natural drug delivery system. We hypothesize that fibrin acts as a biological glue covering Paclitaxel deposits following balloon delivery. In this study, we aimed to evaluate the effect of the number of balloon inflations on luminal fibrin deposits over time.
Methods: A total of 22 porcine femoral arterial segments were randomized to 1x (n=4), 2x (n=7) and 6x (n=11) PCB inflations (Cotavance, Medrad, Inc. Indianola, PA) and followed for 7 days. Additional 7 arterial segments received 6x PCB inflations and were followed for 14 (n=2) and 30 days (n=5). Vessels were harvested for the evaluation of luminal fibrin deposition using a semi-quantitative score.
Results: A total of 148 vessels segments were analyzed in the 7 day study (1x, n=35; 2x, n=37; 6x, n=76) and 40 slides in the long term study (14 days, n=11; 30 days, n=29). Fibrin deposits when present, were found to be deposited on the luminal surface of the vessel and covering crystalline material. At 7 days following PCB inflation, fibrin scores significantly increased according to the number of inflations. Single PCB inflation showed the lowest fibrin score (0.2±0.5) followed by double PCB inflation (0.43±0.55). Six inflations showed a significantly increase in fibrin score (1.88±0.71, p <0.001). In the analysis of PCB over time, a peak in fibrin deposition was seen at 14 days (2.45±1.04) before it decreases at 30 days (1.66±0.90).
Conclusions: Our study suggests that fibrin gets deposited on the surface of the vessel in a dose dependent fashion following PCB delivery and may play a major role in the creation of drug reservoirs and long term intra-vessel drug delivery. The course of the luminal fibrin deposition overtime suggests that this process peaks at 14 days and starts to resorb thereafter.

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Angiographic and clinical outcome in the treatment of Restenosis of Drug Eluting Stents with drug coated balloons in diabetics: Insights from the PEPCAD-DES study

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Background: The PEPCAD-DES Study showed a significantly lower late loss with the use of a drug coated balloon in comparison (SeQuent Please balloon catheter (B.Braun Melsungen AG, Germany) in comparison to balloon angioplasty alone in the treatment of instent-restenosis of drug-eluting stents (DES). In the presence of diabetes there are higher rates of ISR reported in comparison to a healthy population. Purpose of this study was to investigate the impact of diabetes mellitus on late lumen loss and angiographic restenosis in patients, who were treated with a drug-cotaed balloon (DCB) in comparison to balloon angioplasty alone (POBA) for instent-restenosis (ISR) of drug-eluting stents (DES).
Methods: 110 patients with an ISR of either Cypher-, Taxus- or XienceV-stent in a native coronary artery with indication for percutaneous coronary intervention were included in six centers in Germany. Exclusion criteria were: acute myocardial infarction, chronic total occlusion, lesion in grafts, bifurcation lesion, left main lesion, restenosis and in-stent restenosis, contraindication for acetylsalicylic acid or clopidogrel. All patients were scheduled for control angiography at 6 months.
Results: 38 patients were randomized to POBA and 72 patients to DCB. Of these 26 (36.1%) pts. of the DCB-group and 13 (34.2%) were diabetics. DCB as compared with POBA significantly reduced late loss in diabetics and non-diabetics, respectively. At angiographic 6 month follow-up late lumen loss (LLL) in patients treated with a DCB (n=22) was 0.51±0.72 mm in diabetics, and 0.39±0.54 mm in non-diabetics (n=42).In patients treated with POBA LLL was 1.45±0.85 mm in the diabetic subgroup and 0.91±0.71 mm in non-diabetics (n=24). Rates of target lesion revascularization(TLR) rates were significantly lower with DCB versus POBA for non-diabetics (15.2% vs. 36.0%; p=0.045), but not for diabetics (15.4% vs. 38.5%; p=0.107) Overall rates of major adverse cardiac events (MACE) were signific.
Conclusions: Paclitaxel coated balloon angioplasty was superior to POBA for treatment of DES-ISR and reduced significantly MACE-rates in diabetics and non-diabetics. DCB effect on late loss was more effective in patients without diabetes.

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